

**REMARKS**

The present response is responsive to the Office Action.

**Status of the Claims**

Claims 1, 3-11 and 21-30 remain pending in this application.

**Election/Restrictions**

The Examiner restricted previously presented new claims 23-30, as being directed to a different method of Group I (claims 1, 3-11 and 21-22). Specifically, the Examiner noted that claims 23-26 require an output channel, which is not required of the method of Group I, and the method of Group I requires reaction zone, which is not required of the method of claims 23-26. Further, the Examiner asserted that the method of claims 27-30 can be used in materially different processes. The method of Group I or the method of claims 23-26. Applicant respectfully disagrees with the present restriction requirement.

The method of claims 23-26 does require a reaction zone (see claim 23, last phrase: "thereby to define a reaction zone ....") Group I requires a reaction zone defined by a section of a curved serpent-like structure, and further flow pass the reaction zone (which means flow exiting the reaction zone). Claims 23-26 more specifically refer to the alternate claim language of "output channel". While Group I does not specifically use the term "output channel", it would be unreasonable to impose restriction requirement between the two sets of claims simply because there is a term missing in one of the two claim sets.

Further, the Examiner asserted that the biochip of claims 27-30 can be used in the method of Group I or the method of claims 23-26. Since it has been demonstrated above that Group I and claims 23-26 should not be subject to restriction, it follows that claims 27-30 likewise should not be subject to restriction, especially if the biochip of claim 27-30 can be used in the method of Group I or the method of claims 23-26 as the Examiner asserted.

Applicant respectfully requests the restriction requirement be withdrawn.

#### Summary of the Invention

The present invention is directed to a novel approach of defining a fixed, constant volume of reaction zone, without the use of physical flow barriers such as valves and the like. In accordance with the present invention, a microfluidic channel includes a serpentine section constant cross section area. Biological probes are immobilized in the serpentine section to react with a sample solution that comes to rest in the serpentine section. In essence, the presence of the immobilized probes defines the reaction zone, and hence the reaction volume, without the presence of any physical boundaries to define the reaction zone or reaction volume.

In operation, the sample solution (e.g., a sample and reagent) is flow passed the serpentine section, and the flow is terminated. The amount of sample solution that remains in the serpentine section reacts with the immobilized probes, within the reaction zone that has no physical boundaries.

Section 112 Rejections

The Examiner rejected claim 1 on the basis that termination of flow is not enabled by the disclosure. Applicant respectfully disagrees.

Applicant respectfully submits that one skill in the art would appreciate the step of terminating flow given the disclosure of the present application as a whole. Referring to paragraph [0023] of the specification, it was stated that "... it does not matter if we deliver 12  $\mu$ l or 15  $\mu$ l of sample to the sample port, only 10  $\mu$ l (constant reaction volume) of solution would reset with the immobilized probes in the reaction zone." Further, in paragraph [0024], it was stated that "[b]y design, the sample and reagent volumes are more than the reaction volume. Therefore, the excessive solution 16, which is outside the reaction zone 22, does not have the opportunity or sufficient incubation time to react with immobilized probes. ... The fluid in microfluidic channels is moved by a pressurizing mechanism, such as pumping, micro-actuator, electro-osmotic force, acoustic wave, voltage gradient, and capillary action, for providing a forward moving fluid. ... This structure of the present biochip design makes it insensitive to the sample or reagent volumes."

The quoted sections suggest that a larger volume flow of fluid (e.g., 12  $\mu$ l or 15  $\mu$ l ) flowing through the reaction zone would nonetheless define a smaller, constant reaction volume (e.g., 10  $\mu$ l). The sample and reagent volumes are more than the reaction volume. Because the immobilization probes are only found in the reaction zone, the excessive solution outside of the reaction zone would not react or have sufficient time to react with the immobilization probes. Accordingly, the reaction zone defines a constant reaction volume that is independent of any physical flow barriers. Referring also to the rest to the specification, it is clear that the sample reagent volumes are transported to the reaction zone that defines a constant reaction volume, and

there will be excessive solution outside of the reaction zone (which contains immobilizing probes). As a result, the reaction zone defines a fixed volume, to make it insensitive to the sample or reagent volumes. This is also illustrated in Fig. 2(a). Accordingly, it is clear that flow of the sample and reagent is terminated to allow the reaction volume in the reaction zone to complete reaction. If the flow does not terminate, then the sample and reagent volumes would continue to pass through the reaction zone, with no fixed, constant reaction volume.

The Examiner rejected claims 1, 3-11, 21 and 22. Specifically, the Examiner rejected claim 1 on the basis that "serpent-like structure" is vague. Applicant respectfully submits that a serpent-like structure is a serpentine structure, i.e., one that has a meandering profile (according to the 10<sup>th</sup> Edition of Merriam Webster's Collegiate Dictionary; serpentine refers to resemblance of a serpent in its form or movement: something that winds sinuously; winding or turning one way and another; having a compound curve whose central curve is convex. A copy of the dictionary page is attached.) In the case of the present invention, the serpentine structure provides a meandering flow path, as understood from the ordinary meaning of the term, and further consistent with its dictionary meaning.

The Examiner rejected claim 6 on the basis that it is unclear where an external magnet is adjacent to the reaction zone. Applicant submits that the use of magnetic beads and an external magnet (outside of the fluid receptacle) to immobilize the magnetic beads in and by itself is well known to one skill in the art. Further, paragraph [0030] and [0031] and Fig. 4 disclose that the magnetic field trap the magnetic beads in the reaction zone, with the magnet installed under the channel (i.e., outside the biochip) as schematically shown in Fig. 4.

With respect to immobilization of biological probes, claim 7 recites that the biological probe is immobilized on a first surface of a first plate (e.g., without the serpent-like microfluidic channels), which is coupled to a second surface of a second plate on which the microfluidic channels are formed. This configuration is shown in reference to Fig. 1 and accompanying disclosure. Once the first and second plates are coupled, the reaction zone is defined where the biological probes are immobilized within the microfluidic channel.

With respect to claim 21 and 22, the Examiner asserted that "pass and beyond" is unclear. Claim 21 recites that the fluid (e.g., sample and reagent) is transported to the reaction zone, pass and beyond the reaction zone. As explained earlier, the fluid that remains in the reaction zone after the flow terminated would undergo reaction processes.

#### Section 102 Rejection - Blackburn

Claims 1, 3-11, 21 and 22 have been rejected as being anticipated by Blackburn. This rejection has been traversed.

On the outset, Applicant notes that the filing priority date of the present application is prior to the publication date of Blackburn. Therefore, Applicant reserves the right to file a declaration to "swear behind" the reference should the need arise. However, in the interest of forwarding this application to early allowance, Applicant is not pursuing such declaration at this point, especially given that the reference can be distinguished herein.

As the Examiner acknowledged in the Office Action, "Blackburn fails to specifically teach termination flow to allow a portion of the fluid to react with the at least one biological probe." As such, Blackburn clearly does not anticipate claim 1.

Further, independent claim 1 requires a section of curved serpent-like structure defining a reaction zone in the microfluidic channel, and a constant and consistent reaction volume defined by the immobilized probe in the reaction zone, independent of physical flow barriers in the microfluidic channel. Blackburn does not disclose a serpent-like flow structure that defines a constant and consistent reaction volume independent of physical flow barriers. As the Examiner acknowledged, Blackburn uses physical valves to provide flow barriers.

Blackburn also discloses an embodiment of an electrophoretic system. By nature of an electrophoretic system, Blackburn discloses a continuous flow system in which fluid continuously flow past immobilized biological probes. To the extent that the region of the immobilized probes may be deemed to be a reaction zone, it nonetheless does not teach terminating flow after the fluid has been transported to the reaction zone, to allow a portion of said fluid to react with the biological probe. Accordingly, claim 1 should be patentable over Blackburn. The remaining dependent claims are likewise patentable.

**CONCLUSION**

In view of all the foregoing, Applicant submits that the claims pending in this application are patentable over the references of record and are in condition for allowance. Such action at an early date is earnestly solicited. **The Examiner is invited to call the undersigned representative to discuss any outstanding issues that may not have been adequately addressed in this response.**

Respectfully submitted,

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Attachment: Dictionary Page